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Title: Routine Surveillance of Asymptomatic Healthcare Personnel for SARS-CoV-2: Not A Prevention Strategy

Running title: Healthcare is not a Bubble

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Introduction

As capacity for SARS-CoV-2 diagnostics has expanded, both with assay types (nucleic acid amplification tests, NAATs, antigen tests, and serology) and specimen collection options (nasopharyngeal, NP; oropharyngeal, OP; saliva; mid-turbinate, MT; anterior nares, AN), interest in use of routine, serial screening of asymptomatic individuals in a variety of settings has expanded. Notably, the use of asymptomatic surveillance in higher education(1) and professional(2) and non-professional athletics(3), has become commonplace, but transmission in these settings has also been observed and linked to lapses in implementation of basic infection prevention practices such as masking and physical distancing.(4-6) Given the considerable interest in asymptomatic surveillance in areas outside of healthcare, the question of the utility of routine screening among healthcare personnel (HCP) in acute care facilities has been raised.
In this focused review, we describe the reported risk of acquisition of infection after HCP exposures to occultly infected patients, the risk acquisition of infection by patients exposed to occultly infected HCP, the prevalence of asymptomatic infection among HCP in settings where screening has been implemented. We also assess the potential role or routine surveillance of asymptomatic HCP to reduce the risk of nosocomial transmission from HCP-to-HCP and HCP-to-patient. We report on the early experience of acute care facilities that have offered screening of asymptomatic HCP outside of confirmed exposures and conclude with considerations for facilities considering offering screening, either "on demand" or as part of routine surveillance.

Risk of HCP Infection after Exposure to Occultly Infected Patients

There has been widespread implementation of multiple infection prevention measures in healthcare facilities, including universal masking of HCP, patients, and visitors, screening for symptoms and exposures and appropriate isolation of patients and visitors, testing of symptomatic patients as well as targeted testing of asymptomatic patients (i.e., after known exposures, prior to or upon admission to a healthcare facility, and prior to specific high-risk procedures) as well as appropriate isolation and use of personal protective equipment (PPE) by HCP for patients with suspected or confirmed COVID-19.(7, 8) In this setting, the risk of transmission from occultly infected patients appears to be low. This assessment is based on several published investigations of exposures to HCP(Table 1), demonstrating association between universal masking and decreasing incidence of infection,(9) as well as seroprevalence

studies that have generally failed to demonstrate an association between caring for patients with suspected or known COVID-19 and HCP infections, but have shown relationships between household contacts(10) and lack of universal mask use when caring for patients.(11) Several healthcare facility clusters of HCP infection, however, have been linked to HCP-to-HCP transmission tied to eating, drinking, carpooling, and other social events during which infection prevention measures were not adhered to.(12-14)

Risk of Patient Infection after Exposure to Occultly Infected HCP

At least one study has systematically approached the risk to exposed patients from occultly infected HCP, estimated at 0.4%. Baker et al identifed exposed patients between March-June 2020.(15) After the study had begun, based on changes in public health guidance, all exposed patients were referred for testing regardless of symptom status. During this time 238 exposed patients were identified, some with more than one exposure, for a total of 253 exposures by a total of 60 HCP. In 87 exposures, neither patient nor HCP were wearing face masks; in 166 exposures, only the HCP was wearing a face mask. Testing for SARS-CoV-2 by PCR was performed in 92/253 exposures, of which two resulted positive; the first exposure included unmasked face-to-face interaction for 30 minutes in the outpatient setting, the second patient was unmasked for 10 minutes with a masked infected HCP, but this patient was also identified as the close contact of a household case, and infection was attributed to the household.

Prevalence of Asymptomatic Infection Among HCP

Some academic health centers have offered testing to asymptomatic HCP without known exposures (i.e, for indications other than those recommended at this time). We are not aware at this time of any such practices that are mandatory, or that require repeated testing. A limited review of existing programs and results to date are provided (Table 2). The overall prevalence among this population is uniformly low and approximates that of institutes of higher education which have implemented routine serial screening—the Massachusetts Department of Public Health, which tracks the 7-day weighted average of tests by molecular methods notes recent percent positive at 0.3%.(16)

Potential Benefits of Asymptomatic HCP Screening

Testing of asymptomatic HCP will identify some infections that will otherwise go undetected due to lack of prompts for evaluation. The impact of identifying those cases on nosocomial infection is not clear; while asymptomatic individuals do transmit infection, available literature suggests that the secondary attack rate from asymptomatic individuals is less than those with symptoms,(17) and more importantly, in the healthcare setting when adherence to infection prevention protocols are in place, the risk of transmission to patients and other HCP, appears low. The effect of identifying occultly infected HCP on reduced transmission in the community or household setting is likely higher because of the types of interactions in households, and household settings have been shown to have the highest rates of secondary transmission.(18) Since HCP infection risk is likely higher in community and household settings than in healthcare settings, then identification of asymptomatic HCP may have its greates effect in limiting transmission in the household setting.

Outside of a potential impact on reducing transmission, there may be non-infection prevention benefits to offering HCP testing, including HCP satisfaction through ease of access and some measure of reassurance. This reassurance of a negative test, however, is short-lived and runs a risk of reducing compliance with necessary infection control procedures.

Potential Downsides of Asymptomatic Screening

Will HCP who test negative for SARS-CoV-2 modify their behaviors in a way that could increase risk of transmission, by engaging in more risky behaviors, such as eating or drinking in close proximity with non-household members? While we are not aware of evidence to support this change in behavior during the current pandemic, observations of lack of compliance with eye protection in our own institutions in settings where inpatients are all tested for SARS-CoV-2 on admission suggest that HCP are assessing risk of transmission from patients and altering their behavior accordingly (i.e., not wearing eye protection when the patient tested negative despite the existing policy to wear eye protection universally).

The risk of false positive results, which have generally been very low in nucleic acid amplification tests (NAAT) but higher with some antigen tests, in such a low prevelance population must also be considered. Facilities will need to decide in advance if all positive results will be considered to be true infection, or if additional assessment of each would be

required to confirm or refute active infection, taking into account the impact on return-to-work status and exposure investigations. We are unaware of data on testing of asymptomatic HCP, where positive tests were confirmed as “true” positives by follow-up serologic tests.

Practical Considerations

There are very practical considerations to any healthcare facility considering offering asymptomatic HCP screening either as voluntary or mandatory programs.

The considerations include the frequency fo testing, the type of assay, the specimen type, and any pooling strategies, all of which will affect the sensitivity of the assay and timing of detection. Observed self-collection may be an option depending on the specimen type and may introduce efficiencies in testing cohorts of HCP at the same time, with appropriate infection prevention protocols in place. Unobserved self-collection should be undertaken with caution given the possibility of poor sample collection and false-negative results. In low prevalence populations, false positives may be a concern, and facilities may consider protocols to follow up positive screening tests with confirmatory or other tests. Facilities may consider whether to offer testing to all HCP or specific groups, however, caution is advised when focusing on those HCP deemed at “higher risk of infection” due to direct patient care, as the most likely source of infection in all HCP is community exposure. Thus focusing on HCP with higher risk of unrecognized community exposures may be considered. Some facilities may alternatively undertake surveillance among HCP in whom infection would pose a greater risk to patients based on the types of interactions or patient populations with whom they interact. This strategy should be considered with caution, again, however, as the risk to exposed patients when infection prevention measures are in place (i.e., universal masking of HCP, daily symptom monitoring, and masking of patients whenever possible), is low.

In addition to the cost of establishing and maintaining a testing program, the additional resources that will be required for contact tracing to identify potential exposures to other HCP or patients due to lapses in infection prevention protocols must be considered. These include staffing and other support in infection prevention programs and occupational health. The demand for testing may exceed budgeted resources.

Summary

The low risk of nosocomial transmission from patient-to-HCP and from HCP-to-patient, as well as low prevalence of asymptomatic SARS-CoV-2 infection among HCP suggests that current infection prevention measures in place are effective. The addition of routine asymptomatic surveillance to decrease transmission in healthcare facilities should not be pursued as a primary infection prevention strategy, and institutions that consider offering such screening will need to consider the many practical implications. With increasing community prevalence across much of the United States, reinforcing the known, effective infection prevention strategies is paramount. Healthcare is not a bubble and routine screening of asymptomatic HCP will not make it one.

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Tables

Table 1. Risk of Infection after HCP Exposure to Occultly Infected Patients							
Publication	Date, Country	Brief description of occultly infected patient and exposure	Details regarding personal protective equipment	HCP exposed, level of risk of exposure	Number of subsequent infections	Details/Limitations	Rate
Ng, *Annals* 2020(19)	February 2020, Singapore	Patient with occult COVID-19 admitted to hospital; developed respiratory distress on HD 2, intubated by emergency airway team; difficult intubation requiring use of video laryngoscope and airway bougie; mechanical ventilation x 3	35 HCP wore surgical masks; 6 wore N95 respirators	41 HCP with exposure to AGP for at least 10 minutes < 2 meters from patient.	0	All HCP isolated for 2 weeks during which they had daily symptom monitoring, twice daily temperature measurements; NP swabs processed by PCR on first day of home isolation (day 1, 2, 4, or 5 after last exposure) and on day 14.	0.0%

		days; NP positive for SARS-CoV-2 upon extubation.					
Burke, *MMWR* 2020(20)	February 2020, United States	Contact tracing of 12 patients with travel-related COVID-19, including 222 HCP with close contact.[b]	Not described.	222	0	Active symptom monitoring during exposure window; only symptomatic exposed individuals were tested for SARS-CoV-2 by PCR. The number of HCP who developed symptoms and were tested is not specified. Authors note that threshold for testing in HCP might be lower than other exposed individuals.	0.0%
Heinzerling *MMWR* 2020[a(21)]	February 2020, United States	Patient managed on standard precautions for 4 days during which	HCP stratified as high, medium and low risk per CDC; risk	121	3	Active symptom monitoring during the exposure window; only symptomatic exposed individuals were tested for	2.5%

		the patient underwent multiple AGPs, including nebulizer treatments, bilevel positive airway pressure, endotracheal intubation, and bronchoscopy; identified as SARS-CoV-2 after transfer to another facility (see Bays et al for exposure investigation of this patient at the second hospital)	stratification provided for 43 who developed symptoms and were tested: high (5), medium (36), and low (2). Among 3 diagnosed with COVID-19, two had high risk (frequent close contact during BiPAP, intubation with no facemask, respirator, gown or gloves) and one had medium risk exposures (close contact for 2 hours wearing a			SARS-CoV-2 by PCR.	

			facemask inconsistently; wearing gloves, no eye protection).				
Bays, ICHE 2020 [a(22)]	February and March 2020, United States	Describes exposure investigation related to 2 occultly infected patients. Patient 1 was transferred on from a community hospital (community hospital exposure is described in Heinzerling et al) to Hospital B. Patient 2 was transferred from another	Patient 1 exposures included high (15), medium (73), and low (59) risk. Patient 2 exposures included high (20), medium (59), and low (66) risk.	147 145	0 5 confirmed 2 possible	Active symptom monitoring during the exposure window; only symptomatic exposed HCP were tested for SARS-CoV-2 by PCR. Active symptom monitoring during the exposure window; symptomatic and a subset of asymptomatic exposed HCP were tested for SARS-CoV-2 by PCR. Of 5 confirmed cases, 4 were present for intubation without adequate PPE, the fifth had direct contact for several days without PPE and during a break in the vent circuit. Two possible cases were among staff	2.4%

		community hospital to Hospital B and was on Standard Precautions for 14 days prior to suspicion for COVID-19 during which the patient was intubated and had bronchoscopy performed.				who had direct patient contact during AGPs without adequate PPE.	
Ghinai , *Lancet* 2020[c](23)	February 2020, United States	Person-to-person spread in household between two patients and report of exposures from those two patients within community and healthcare setting	Not described however, healthcare exposures from Patient 2 are noted in non-hospitalized settings as the patient was appropriately	75	0	Active symptom monitoring during the exposure window; symptomatic exposed individuals were tested for SARS-CoV-2 by PCR; a subset of asymptomatic HCP were tested.	0.0%

			isolated upon admission.				
Cheng, *JAMA IM* 2020(24)	January – March 2020, Taiwan	Prospective case study of confirmed COVID-19 patients and their close contacts; 698 close contacts were identified in healthcare settings.	Close contact defined as contacting the index case within 2m without appropriate PPE; no minimum time requirement. Appropriate PPE depended on the exposure setting; during AGPs, N95 required.	698	6	Active symptom monitoring during the exposure window; symptomatic exposed individuals were tested for SARS-CoV-2 by PCR; asymptomatic HCP were also tested as they were considered high-risk population. Repeat testing of asymptomatics only conducted if symptoms developed during the exposure period.	0.9%
Baker, *ICHE* 2020(25)	March 2020, United States	Patient admitted to hospital and on Standard Precautions through HD 13 at which point he developed acute	Close contacts defined as ≥ 10 cumularive minutes of face-to-face contact within 2m. Median	43	2	Active symptom monitoring; all exposed HCP were offered testing for SARS-CoV-2 by PCR, regardless of symptoms. 8 of 44 developed symtpoms and 3 tested positive. Of 36 asymptomatic HCP, 29 were	4.7%

		respiratory failure; determination made that he was likely infected at the time of admission. The patient was not wearing a mask; on HD7, a new universal masking policy went into effect and HCP work surgical masks.	cumulative time with patient was 45m (range 10-720min)			tested and all negative. Note that one HCP who was identified as infected was determined to have a household exposure and thus was removed from denominator and numerator for calculation.	
						Average	**1.2%**

HD: hospital day; NP: nasopharyngeal; PCR: polymerase chain reaction; HCP: healthcare personnel; AGP: aerosol-generating procedure;

[a] "Hospital A" referred to in Heinzerling et al is described in detail in Bays et al, where Hospital B is also described. Data presented for Heinzerling include only those from "Hospital A." Data included from Bays et al pertains to Hospital B contact tracing investigation (investigation 1A and 2).

[b] Close contact defined by CDC at the time: "Examples of close contact with a patient or with infectious material could include spending prolonged time within 6 feet of the patient, conducting or being present during an aerosol-generating procedure, or direct contact with the patient's secretions or excretions."

[c] Exposures related to patient 2 are included in this table because Patient 1 was described in Burke et al; 75 unique HCP contacts are included (Personal communication from R Burke to E Shenoy, 8/19/2020).

Table 2. Reported Prevalence of SARS-CoV-2 Infection Among Asymptomatic HCP						
Location, start date	Brief description	Total tests performed	Number of cases detected	Rate	Type of test	Reference
Brigham and Women's Hospital, 9/25/2020[a]	Asymptomatic employees, initiated as part of a hospital cluster, though offered broadly to all employees on campus.	10,840 in 7,999 HCP	14	0.2%	Dry AN swab, self-collected, processed by PCR	(26)
Massachusetts General Hospital; 10/27/2020	Asymptomatic employees without known exposure are offered voluntary testing, free of charge; limit one per week.	5,081 HCP	21	0.4%	Dry AN swab, self-collected, processed by PCR	(27)
National Institutes of Health; patient care providers 5/21/2020; NIH campus 8/11/2020	Asymptomatic testing is voluntary but highly encouraged; clinical staff are encouraged to test weekly. Pooled specimen approach is used.	38,450 in 8,578 HCP	33	0.4%	Initially NP swab; beginning 9/14/2020 saliva; mid-turbinate also accepted; processed by PCR	(28)
University of California San Francisco, 7/2020	Voluntary testing of asymptomatic employees, trainees, and students randomly selected. Offered in addition to asymptomatic testing for	16,702 in 7,627 HCP	[b]	0.21%	Self-administered, observed, AN	(29, 30)

	new and returning trainees and students, new campus housing tenants, child care staff working in UCSF's child care centers, and others.					
Yale New Haven Health System, June-July 2020	Voluntary testing of asymptomatic healthcar workers	11,000	28	0.25%	Details not available	(31)

HCP: healthcare personnel; AN: anterior nares; NP: nasopharyngeal.

[a] screening was initiated in the setting of a cluster of infections though vast majority of testing was performed in non-exposed HCP. Total infections presented are those that were not attributed to the cluster and these 14 were removed from the denominator for calculation of proportion positive.

[b] Data provided to not allow identification of asymptomatic denominator.

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